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Pregnancy rate after vasectomy reversal in a contemporary series: influence of smoking, semen quality and post-surgical use of assisted reproductive techniques

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Study Type – Outcomes (cohort series)
Level of Evidence 2b

OBJECTIVE

- To determine the influence of smoking, postoperative semen characteristics and the use of an assisted reproductive technique (ART) on pregnancy rate in a contemporary series of men undergoing vasectomy reversal.

PATIENTS AND METHODS

- Between January 2002 and January 2009, 186 vasectomy reversals were performed. Of the 171 patients who could be contacted for follow-up, 162 attempted pregnancy and constitute the study group.
- Semen analysis was performed 3 months after the procedure and at subsequent 3-monthly intervals.
- Patient characteristics and surgical information were obtained from a computerized database, and follow-up data were collected by telephone interview.
- A multivariate Cox regression model was used to discern possible prognosticators with respect to pregnancy outcome.

What's known on the subject? and What does the study add?

Microsurgical vasectomy reversal is an effective and cost-effective method of reinstating fertility in a man who has previously had a vasectomy. The current literature indicates that the success rate (i.e. potency and pregnancy rates) are dependent primarily on the time elapsed since vasectomy and the age of the female partner.

Using a multivariate Cox regression model, evaluation of the influence of preoperative data (including smoking) and semen parameters indicates a significant influence of post-surgical sperm motility only, on time to first pregnancy. The use of assisted reproductive techniques, when natural pregnancy failed, was successful in ~50% of couples who attempted this procedure and accounted for an absolute increase in pregnancy rate of 14%.

RESULTS

- The overall patency rate was 91.4%, with a natural pregnancy rate of 44.4% and a subsequent 14.2% of patients conceiving using a ARTs resulting in a total pregnancy rate of 58.6%. Multiple pregnancies were obtained by 20.4% of couples.
- Smoking of the male or female partner did not influence the probability of conception.
- In a multivariate model that included, among other factors, time since vasectomy, female age and semen characteristics, only sperm motility was significantly related to natural pregnancy outcome.
- The probability of obtaining a natural pregnancy within 2 years after surgery is 53% for men with sperm motility >20%

(WHO a+b) compared to 19% for men with sperm motility <5% ($P = 0.003$).

CONCLUSIONS

- A clear and significant association between sperm motility and the probability of conception was found, whereas smoking, female age and time since vasectomy appeared to have no influence on pregnancy outcome in this patient cohort.
- The use of ARTs accounted for an absolute increase in pregnancy rate of 14.2%.

KEYWORDS

ART, motility, pregnancy, smoking, sperm, vasectomy reversal

INTRODUCTION

In an era where surgical sperm retrieval and intracytoplasmic sperm injection (ICSI) are commonplace, many couples who wish to conceive after the male partner has had a

vasectomy will still opt for vasectomy reversal. Considerations are the success rate, cost-effectiveness, the obtainment of one or multiple 'natural' pregnancies, and avoidance of the burden of treatment of a healthy female partner [1].

A number of factors have been shown to influence the probability of conception after vasectomy reversal. Among these, microscopic technique, time since vasectomy and female partner age were all shown to have a significant effect [2–5]. Other factors,

such as DNA fragmentation, and, unexpectedly, postoperative semen parameters have not been shown to be important prognosticators for pregnancy [2,5,6].

Presently, couples who wish to conceive after a vasectomy reversal may have their probability of a pregnancy inadvertently influenced by the many factors that a modern society has to offer. Among these, smoking may have a negative influence [7,8], whereas the use of a readily available assisted reproductive technique (ART) may increase postoperative pregnancy rates, especially in eager and motivated couples. To better understand these influences, and in light of the willingness of many couples to turn to ARTs when the postoperative probability of a natural pregnancy is perceived as slim, the present study analyzed the effect of cigarette smoking and the prognostic relevance of postoperative semen parameters in this contemporary series. The frequency and success of the postoperative use of ARTs was also investigated.

PATIENTS AND METHODS

All patients undergoing a primary or repeat vasectomy reversal procedure at the Department of Urology of St Elisabeth Hospital (Tilburg, the Netherlands), between January 2002 and January 2009, were reviewed. Standard data, including age, medical history and surgical information, were obtained from the available charts. Follow-up data, including pregnancies, use and timing of ARTs, and smoking habits, were collected by telephone interview, using a standardized questionnaire.

Surgery was performed under general anaesthesia. Before reconstruction, efflux of the proximal vas portion was evaluated for gross appearance and microscopic presence of sperm. If clear watery efflux or any efflux containing whole sperm was found, vaso-vasostomy (v-v) using a modified one-layer technique was performed using 9-0 ethylon sutures. If thick white ('toothpaste-like') or milky fluid containing no sperm or only sperm heads was found, vaso-epididymostomy (v-e) using a two stitch intussusception technique was performed with 10-0 ethylon sutures. Patients were released on the day of surgery

and were advised to rest at home for 1 week before resuming regular activities.

Patients were advised to submit semen for analysis 3 months after surgery. In cases of patency, patients were advised to perform semen analysis every subsequent 3 months during the first year after reversal or until pregnancy to identify the possible occurrence of secondary obstruction. If a unilateral or bilateral v-e was performed, 3-monthly analyses were also performed in patients with persistent azoospermia because the time to patency may be much longer than 3 months after surgery [9]. Patency is defined as the presence of any sperm with tails (with or without motility) in the ejaculate. For purposes of the present study, the absence of sperm at first analysis is regarded as failure for v-v procedures, and couples were advised to turn to ARTs with surgically obtained sperm. In cases of unilateral or bilateral v-e, azoospermia at first analysis was regarded as failure; however, patients were advised to wait 1 year, performing 3-monthly semen analyses and, if at any subsequent analysis sperm were found in the ejaculate, the notation of failure was changed to patency.

Smoking habits included the smoking any amount of cigarettes during recovery from surgery and during attempted pregnancy for both men and their partners.

Semen analysis was performed within 2 h after production of the sample at our *in vitro* fertilization laboratory according to criteria specified by WHO [10].

STATISTICAL ANALYSIS

Statistical analyses were performed using PASW Statistics, version 17 (SPSS Inc., Chicago, IL, USA).

Baseline characteristics of the participants with respect to the pregnancy status at the end of the study were examined. Pregnancy status was defined as success if a couple obtained at least one pregnancy. The chi-squared test was used to compare categorical characteristics, whereas a *t*-test for independent samples was used to compare the success and failure groups on baseline continuous characteristics such as age.

A series of Cox regression models was fitted using the baseline measurements to determine the univariate effect of each variable on the success of pregnancy over time. Next, a multivariate Cox regression model was fitted, including all baseline characteristics simultaneously.

$P < 0.05$ (two-sided) was considered statistically significant.

RESULTS

SUBJECTS CHARACTERISTICS AND PREGNANCIES

Between January 2002 and January 2009, 186 vasectomy reversals were performed.

Of these, 171 could be contacted for follow-up, 162 of whom attempted pregnancy. The latter group constitutes the study group. Follow-up after vasectomy reversal was at least 1 year with a mean and median of 3.4 and 2.9 years, respectively.

The characteristics of patients and their partners stratified by outcome as a success or failure with pregnancy are depicted in Table 1. Among 162 men in the study, 48 (29.6%) were smokers, whereas 41 (25.3%) partners smoked. Mean (SD) ages were 42.6 (5.9) years and 32.4 (4.9) years for men and partners, respectively. Mean (SD) interval period after vasectomy was 7.9 (4.4) years at the time of reversal surgery. The surgical procedure consisted of a bilateral v-v in 110 (67.9%) patients, unilateral v-v in five (3.1%) patients, a bilateral v-e in 19 (11.7%) patients, a unilateral v-e in six (3.7%) patients and a combination of unilateral v-v and v-e in 22 (13.6%) patients.

Overall patency was 91.4%. For each type of surgical procedure, the pregnancy rates are shown in Table 1. Secondary reconstructive procedures were performed in 16 (9.9%) patients with a patency rate of 92.3%. Of these, 68.8% required v-e on at least one side compared to 24.6% of primary procedures.

Of the men who smoked, 54.2% achieved at least one pregnancy, whereas this percentage was 60.5% among non-smokers. The difference is not statistically significant (chi-squared, $P = 0.453$). There was also no difference in pregnancy rate between

TABLE 1 Summary of baseline characteristics by pregnancy success at the end of the study

Characteristic	<i>n</i> (%)	Pregnant (%)		<i>P</i>
Total	162	58.6		
Smoker				
No	114 (70.4)	60.5		0.453
Yes	48 (29.6)	54.2		
Partner smoker				
No	121 (74.7)	58.7		0.987
Yes	41 (25.3)	58.5		
Surgical procedure				
W-W	100 (67.9)	58.2		0.456
W	5 (3.1)	80.0		
VE-VE	19 (11.7)	52.6		
VE	6 (3.7)	33.3		
W-VE	22 (13.6)	68.2		
	Combined, mean (SD)	Pregnant, mean (SD)	Not pregnant, mean (SD)	<i>P</i>
Age (years)	42.60 (5.89)	42.0 (5.3)	43.5 (6.6)	0.127
Partner age (years)	32.35 (4.86)	32.0 (5.0)	32.9 (4.6)	0.254
Vasectomy interval (years)	7.89 (4.4)	7.49 (4.18)	8.38 (4.77)	0.209

v-e, vaso-epididymostomy; v-v, vaso-vasostomy.

TABLE 2 Mean semen parameters after vasectomy reversal for smokers and non-smokers and the *P* value of the *t*-test for independent samples

Semen parameter	Smoker	Non-smoker	P
Volume (mL)	3.06	3.07	0.97
Concentration (millions/mL)	22.36	22.92	0.92
Total motility (%)	23.42	29.48	0.06

smoking and non-smoking women. Interestingly, further analysis (data not shown) for the obtainment of a second pregnancy showed a significantly lower number of second pregnancies in couples where the female partners were smokers (Mann-Whitney *U*-test, $P < 0.01$).

No significant difference between the percentages of pregnancies between the surgical procedures was found; however, the numbers in certain groups were small.

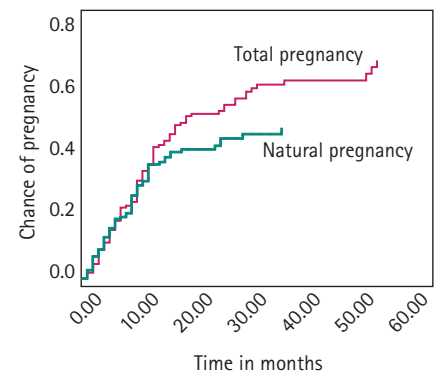
The mean ages of men and partners those who had pregnancy were not significantly lower than the mean ages of those who did not succeed in pregnancy. The interval since vasectomy was also not significantly shorter for those who obtained a pregnancy.

INFLUENCE OF SMOKING ON SEMEN PARAMETERS

Postoperative semen volume and sperm concentration were not related to the smoking status of patients (Table 2). Even though the total sperm motility among smokers was lower than that of non-smokers, the difference was not statistically significant ($P = 0.06$).

NATURAL VERSUS ART METHODS

Overall, 137 pregnancies occurred in the study group. There were 95 couples (58.6%) who achieved at least one pregnancy, whereas multiple pregnancies were achieved by 33 (20.4%) couples. Of first pregnancies ($n = 95$), 75.8% were natural; of second pregnancies ($n = 33$) 54.5% were natural;

FIG. 1. Probabilities of natural and total (natural + assisted reproductive technique) pregnancies over time.

and, of third pregnancies ($n = 9$), 44.4% were natural. The use of ARTs was attempted by 49 (30.2%) couples of whom 23 (46.9%) subsequently conceived. For couples who underwent ARTs, the mean (SD) time to first ART use was 13.9 (10.8) months. Among all patients, 23 (14.2%) conceived using ARTs, whereas 72 (44.4%) conceived naturally.

Figure 1 shows the probability of pregnancy at different times for all pregnancies and for natural pregnancies only. Mean (SD) overall time to first pregnancy was 11.85 (10.7) months. Mean (SD) time to pregnancy was shorter for those couples who did not (need to) use ARTs vs those who did: 9.2 (8.4) months vs 21 (12.7) months ($P < 0.001$).

PREDICTORS OF PREGNANCY

A Cox regression model was fitted to determine the influence of a number of parameters on the time to first pregnancy. In the study group, only sperm motility had a significant positive influence ($P < 0.001$), whereas all other variables (i.e. age, partner's age, time since vasectomy and smoking status of both male and partners) were not significantly related to time to first pregnancy. Sperm motility was considered as a continuous variable in this last Cox regression model. Next, three groups of the variable sperm motility were constructed to facilitate the interpretation of the results from the Cox regression model. The first group consisted of patients with a sperm motility (WHO a+b) value $\leq 5\%$, the second group consisted of those with value in the range 5–20% and the last group consisted

TABLE 3 Multivariate Cox regression model aiming to identify predictors of the pregnancy rate over time

Characteristic	Hazard ratio	95% CI	P
Smoker	0.78	0.45–1.37	0.395
Partner smoker	1.34	0.76–2.36	0.318
Age (years)	1.00	0.95–1.05	0.911
Partner age (years)	1.00	0.96–1.04	0.992
Vasectomy interval	1.00	0.99–1.01	0.363
Surgical procedure (v-e)	0.53	0.24–1.18	0.118
Sperm concentration	1.00	0.99–1.09	0.594
Total forward motility (>20% as reference group)			
Between 5% and 20%	0.50	0.246–1.028	0.060
<5%	0.28	0.119–0.652	0.003

v-e, vaso-epididymostomy.

of the remaining patients with a motility >20%. Groups 1, 2 and 3, comprised 18%, 16% and 66% of the study population respectively. Using this newly-defined group variable for motility and all other variables, a Cox regression model that considers time to natural pregnancy as dependent variable was fitted and the results are shown in Table 3.

Table 3 shows that only the sperm motility variable was significantly related to the probability of natural pregnancy over time after controlling for all other variables in the model. The group with a motility >20% was considered as the reference group. The probability of natural pregnancy for the second group with a motility in the range 5–20% was not statistically different from the reference group ($P = 0.06$), whereas the group with a motility <5% was significantly different from the reference group ($P = 0.003$). The hazard ratio shows that the 'risk' of obtaining a natural pregnancy when motility is <5%, is ≈ 0.278 compared to the reference group, whereas the hazard ratio is ≈ 0.5 for the group with a motility in the range 5–20% compared to the reference group.

Figure 2 depicts the probability of natural pregnancy over time for the three groups of sperm motility. At 24 months after surgery, the group with a sperm motility >20% had a 53% probability of obtaining a natural pregnancy, whereas the corresponding probabilities were 31% and 19% for the groups with a motility in the range 5–20% and below 5%, respectively.

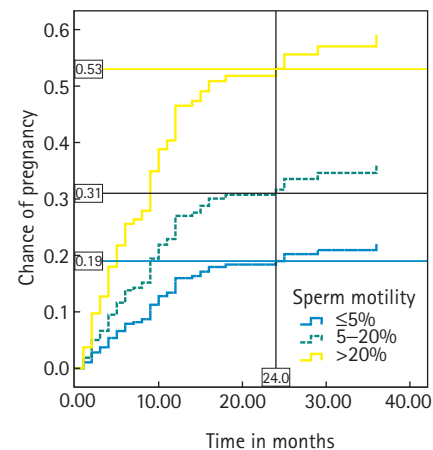
DISCUSSION

Couples who have decided to attempt a pregnancy when the male partner has previously been sterilized are routinely offered a choice between vasectomy reversal and surgical sperm retrieval with ICSI. Because of the high success rate of contemporary vasectomy reversal techniques, cost-effectiveness and the necessity of subjecting a healthy young woman to invasive procedures in the case of ICSI treatment, the first option is often chosen. After surgery, further decisions may need to be made (i.e. at first semen analysis, when the quality of semen is perceived as dismal, and possibly after some time, often at least 1 year, if no natural pregnancy has yet occurred). Thus, even after vasectomy reversal, the choice to invoke ARTs is ever present and may indeed be prudent in cases where the probability of a natural pregnancy is limited.

For the physician, it is important to understand the factors that influence the probability of conception and to be able to apply this knowledge to individual couple counselling.

A number of previous studies have indicated a negative correlation between the time since vasectomy and postoperative patency and the probability of pregnancy [2,3,5]. An increase in time since vasectomy was associated with unfavourable intra-operative fluid findings and an increase in the incidence of the need for v-e. Interestingly, the recent literature has indicated that

FIG. 2. Probabilities of natural pregnancy stratified by three motility groups over time. The points at which the horizontal lines within the plot cross the vertical line at 24 months show the probability of natural pregnancy at 2 years after surgery for each group; the probability is 0.53 (53%) for the group with a motility >20% (WHO a+b). The probability of natural pregnancy is 31% for the group with a motility in the range 5–20%. The probability of natural pregnancy is 19% for the group with a motility <5%.



intra-operative fluid findings are no measure for postoperative patency but may predict the probability of pregnancy [11]. Furthermore, the associations between time since vasectomy with lower patency and pregnancy rates were not found in a recent study by Boorjian *et al.* [12] up to 15 years after vasectomy. In that study, it was argued that contemporary microscopic techniques and higher v-e success rates increase the success rates in men with a longer interval. The results obtained in the present study concur with the latter findings. Time since vasectomy was not a predictive factor in a multivariate analysis for time to first pregnancy.

Another important factor has traditionally been the age of the female partner. Previous studies have found a profound effect of age on pregnancy after vasectomy reversal in women aged >40 years [2–5]. No such influence could be found in a multivariate analysis; however the mean (SD) age of the women in the present study was 32.4 (4.9) years, and the number of women aged ≥ 40 years was limited ($n = 8$; 5%).

There were 16 men who had undergone a previous vasectomy reversal. A number of

studies have shown repeat procedures to be successful in a large percentage of cases [13]. The findings of the present study concur with that data. There were 92% of secondary procedures that resulted in patency, with 56.3% and 75% natural and total pregnancies, respectively.

A number of lifestyle factors may be of importance in obtaining a pregnancy after vasectomy reversal. The present literature indicates that smoking, especially in the female partner, may have a profound negative influence on pregnancy rates during *in vitro* fertilization [7,8]. According to a recent meta analysis by Waylen *et al.* [8], 'There is particularly overwhelming evidence for a decreased clinical pregnancy rate amongst [female] smokers, in addition to the strong implication of a negative effect on live birth rate, miscarriage rate, ectopic pregnancy rate and fertilization rate'. With respect to the occurrence and timing of the first pregnancy, no association between smoking and pregnancy outcome was found in the present study. Nor was there any effect of smoking by the male partner on postoperative semen parameters. Interestingly, there was a significant decrease in the occurrence of a second pregnancy in smoking women. It is not immediately clear what biological phenomenon may be at the root of this finding. An observation by Sharara *et al.* [14] indicates that the ovarian reserve may be compromised by smoking, which would increase the effect of smoking on fertility as the age of the female partner progresses, and may ultimately leave smoking women with fewer offspring. It could also be argued that smoking may be indicative of other lifestyle factors, which in turn could affect the decision to attempt a second pregnancy.

Semen analysis is the cornerstone of the clinical measure of a man's fertility. Although imperfect, very poor semen values are invariably associated with lower pregnancy rates in couples who are trying to conceive. Unexpectedly, such associations have not been reported for the pregnancy rates of men after vasectomy reversal. In the present study cohort, the sperm concentration after surgery was not related to pregnancy outcome. Sperm motility was, however, highly predictive of postoperative conception. This finding held true in a multivariate model. If, 3 months after

vasectomy reversal, sperm motility is <5% (WHO a+b), the hazard ratio of conception compared to a man with sperm motility >20% is 0.278 ($P < 0.003$), representing a probability of conception of 19% and 53% after 2 years of unprotected intercourse for a motility <5% and a sperm motility >20%, respectively (Fig. 2). Not all men will induce a pregnancy after vasectomy reversal. ARTs may therefore be of value in selected couples. The challenge lies in the identification of those patients who will most probably benefit from this technology and when to invoke it. In our experience, the failure of a natural pregnancy to occur after some time will induce some of these highly motivated couples to seek 'other options'. This is most poignant for women approaching the age of 40 years. There is presently no guideline when, after vasectomy reversal, ARTs should be considered and, often, decisions are based on arbitrary and emotional factors. It appears reasonable to consider ARTs when pregnancy fails to occur within 1–2 years after surgery, as is the case in 'regular' infertile couples. We advise our patients to have postoperative 3-monthly semen analyses, aiming to rule out secondary obstruction, in which case ARTs may be warranted without further delay. The data obtained in the present study indicate that, in addition to the above considerations, ARTs may also be indicated in cases where postoperative sperm motility is very low.

Intra-operative sperm retrieval using microsurgical sperm aspiration or testicular sperm extraction (TESE) was not performed in the present patient cohort for two reasons. First, viable sperm retrieval, although possible during v-e, otherwise usually requires either the puncture of an intact epididymis or testicular sperm extraction, which could have an impact on patency in the first case or risk any of the sequelae of damaging an intact testis, including anti-sperm antibody formation or the creation of a hematoma. Second, cryopreservation of sperm is costly and is not reimbursed in the Netherlands, whereas the most couples who opt for ARTs are able to use ejaculated sperm. If necessary, sperm retrieval can be performed relatively easily in an outpatient setting using local anaesthesia.

The present study is limited in its retrospective design and the relatively small

cohort of patients included. Nevertheless, although smoking, time since vasectomy and female age were not related to pregnancy in the present study cohort, a clear and significant association between postoperative sperm motility and the probability of conception was shown. In addition, in the present series, the availability and use of ARTs after vasectomy reversal resulted in an absolute increase in pregnancy rate of 14.2%.

CONFLICT OF INTEREST

None declared.

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Abbreviations: ART, assisted reproductive technique; ICSI, intracytoplasmatic sperm injection; v-e, vaso-epididymostomy; v-v, vaso-vasostomy.